

CLAIMS

1. A set of genetic polymorphisms being associated with optic neuropathy, which comprises at least one polymorphism selected from the group consisting of:

- 5 (1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);
- (2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;
- (3) A138 insertion/deletion(A138I/D) polymorphism in exon 1
10 of the Endothelin-1 gene;
- (4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;
- (5) +1222C>T polymorphism of the Endothelin Receptor A gene;
- 15 (6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);
- (7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;
- (8) CTG to CTA substitution at codon 277 in exon 4 of the
20 Endothelin receptor B gene;
- (9) 9099C>A polymorphism of the Mitochondrial gene;
- (10) 9101T>G polymorphism of the Mitochondrial gene;
- (11) 9101T>C polymorphism of the Mitochondrial gene;
- (12) 9804G>A polymorphism of the Mitochondrial gene;
- 25 (13) 11778G>A polymorphism of the Mitochondrial gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

5 (25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

10 (27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);

(32) GGA to CGA substitution at codon 389 of the β 1 adrenergic receptor gene (Gly389Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

15 (37) 1402C>T polymorphism of the E-Selectin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

20 (39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor α gene promoter region and 603T>A of the Optineurin gene;

(40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro);

25 (41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrolase 1 gene (Tyr113His);

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

5 (44) -670A>G polymorphism of the CD95 gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the β 2 adrenergic receptor gene (Gly16Arg); and

10 (48) CAA to GAA substitution at codon 27 of the β 2 adrenergic receptor gene (Gln27Glu).

2. A method for diagnosing or predicting susceptibility to optic neuropathy in a human subject, which comprising the steps of:

15 i) obtaining a biological sample from the subject,

ii) determining genotype of the sample in respect of the set of the polymorphisms of claim 1, and

iii) diagnosing or predicting susceptibility to optic neuropathy in the subject based on the genotype.

20 3. The method of Claim 2, wherein the optic neuropathy is glaucoma or Leber's disease.

4. The method of Claim 2, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with
25 optic neuropathy.

5. A method for diagnosing or predicting susceptibility to glaucoma in a human subject, which comprising the steps of:

i) obtaining a biological sample from the subject,

5 ii) determining genotype of the sample in respect of a set of polymorphisms comprising at least one polymorphism selected from the group consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

10 (2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

(3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;

15 (4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

(5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

20 (7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

(8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;

(9) 9099C>A polymorphism of the Mitochondrial gene;

25 (10) 9101T>G polymorphism of the Mitochondrial gene;

- (11) 9101T>C polymorphism of the Mitochondrial gene;
(12) 9804G>A polymorphism of the Mitochondrial gene;
(13) 11778G>A polymorphism of the Mitochondrial gene;
(14) -713T>G polymorphism of the Angiotensin II type 1
5 receptor gene promoter region;
(16) 3123C>A polymorphism of the Angiotensin II type 2
receptor gene;
(25) CAA to CGA substitution at codon 192 of the
Paraoxonase 1 gene (Gln192Arg);
10 (26) TTG to ATG substitution at codon 55 of the Paraoxonase
1 gene (Leu55Met);
(27) CGG to CAG substitution at codon 144 of the Noelin 2
gene (Arg144Gln);
(32) GGA to CGA substitution at codon 389 of the β 1
15 adrenergic receptor gene (Gly389Arg);
(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);
(36) 412G>A polymorphism of the Optineurin gene;
(37) 1402C>T polymorphism of the E-Selectin gene;
(38) The combination of polymorphisms of -857C>T of the
20 Tumor necrosis factor α gene promoter region and 412G>A of
the Optineurin gene;
(39) The combination of polymorphisms of -863C>A of the
Tumor necrosis factor α gene promoter region and 603T>A of
the Optineurin gene;
25 (42) -110A>C polymorphism of the Heatshock protein 70-1

gene promoter region;

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

5 (45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the β 2 adrenergic receptor gene (Gly16Arg); and

10 (48) CAA to GAA substitution at codon 27 of the β 2 adrenergic receptor gene (Gln27Glu), and

iii) diagnosing or predicting susceptibility to glaucoma in the subject based on the genotype.

6. The method of Claim 5, wherein the set of polymorphisms further comprises at least one genetic
15 polymorphism which has been known to be associated with glaucoma.

7. The method of Claim 5, wherein the at least one genetic polymorphism is selected from the group consisting of:

20 (1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

(2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

25 (5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

5 (16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

10 (32) GGA to CGA substitution at codon 389 of the β 1 adrenergic receptor gene (Gly389Arg);

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys), and

15 the glaucoma is normal tension glaucoma.

8. The method of Claim 7, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with normal tension glaucoma.

20 9. The method of Claim 5 wherein the at least one genetic polymorphism is selected from the group consisting of

(4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

25 (14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

5 (38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

10 (44) -670A>G polymorphism of the CD95 gene promoter region;

(47) GGA to AGA substitution at codon 16 of the $\beta 2$ adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the $\beta 2$ adrenergic receptor gene (Gln27Glu), and

15 the glaucoma is primary open angle glaucoma.

10. The method of Claim 9, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with primary open angle glaucoma.

20 11. A method for diagnosing or predicting susceptibility to Leber's disease in a human subject, which comprising the steps of:

i) obtaining a biological sample from the subject,

ii) determining genotype of the sample in respect of

25 the set of the polymorphisms comprising at least one

polymorphism selected from the group consisting of:

(40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro); and

(41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrolase 1 gene (Tyr113His), and

iii) diagnosing or predicting susceptibility to Leber's disease in the subject based on the genotype.

12. The method of Claim 11, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with Leber's disease.

13. The method of any of Claims 2-12, wherein the genotype is determined by the method selected from the group consisting of polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP) analysis, polymerase chain reaction followed by single strand conformation polymorphism (PCR-SSCP) analysis, ASO hybridization analysis, direct sequencing analysis, ARMS analysis, DGGE analysis, RNaseA cleaving analysis, chemical restriction analysis, DPL analysis, TaqMan® PCR analysis, Invader® assay, MALDI-TOF/MS analysis, TDI analysis, single nucleotide extension assay, WAVE assay and one molecular fluorescent detection assay, and a mixture thereof.

14. A kit for diagnosing or predicting susceptibility to optic neuropathy in a human subject which comprises primer

set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

- 5 (1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);
- (2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;
- (3) A138 insertion/deletion(A138I/D) polymorphism in exon 1
10 of the Endothelin-1 gene;
- (4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;
- (5) +1222C>T polymorphism of the Endothelin Receptor A gene;
- 15 (6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);
- (7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;
- (8) CTG to CTA substitution at codon 277 in exon 4 of the
20 Endothelin receptor B gene;
- (9) 9099C>A polymorphism of the Mitochondrial gene;
- (10) 9101T>G polymorphism of the Mitochondrial gene;
- (11) 9101T>C polymorphism of the Mitochondrial gene;
- (12) 9804G>A polymorphism of the Mitochondrial gene;
- 25 (13) 11778G>A polymorphism of the Mitochondrial gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

5 (25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

10 (27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);

(32) GGA to CGA substitution at codon 389 of the β 1 adrenergic receptor gene (Gly389Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

15 (37) 1402C>T polymorphism of the E-Selectin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

20 (39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor α gene promoter region and 603T>A of the Optineurin gene

(40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro);

25 (41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrolase 1 gene (Tyr113His);

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

5 (44) -670A>G polymorphism of the CD95 gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the β 2 adrenergic receptor gene (Gly16Arg); and

10 (48) CAA to GAA substitution at codon 27 of the β 2 adrenergic receptor gene (Gln27Glu).

15. The kit of Claim 14, wherein the optic neuropathy is glaucoma or Leber's disease.

16. The kit of Claim 14, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with optic neuropathy.

17. A kit for diagnosing or predicting susceptibility to glaucoma in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

25 (2) -1370T>G polymorphism of the Endothelin-1 gene promoter

region;

(3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;

(4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

(5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

(8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;

(9) 9099C>A polymorphism of the Mitochondrial gene;

(10) 9101T>G polymorphism of the Mitochondrial gene;

(11) 9101T>C polymorphism of the Mitochondrial gene;

(12) 9804G>A polymorphism of the Mitochondrial gene;

(13) 11778G>A polymorphism of the Mitochondrial gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(26) TTG to ATG substitution at codon 55 of the Paraoxonase

1 gene (Leu55Met);

(27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);

5 (32) GGA to CGA substitution at codon 389 of the β 1 adrenergic receptor gene (Gly389Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

(37) 1402C>T polymorphism of the E-Selectin gene;

10 (38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

(39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor α gene promoter region and 603T>A of the Optineurin gene;

15 (42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

20 (45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene (Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the β 2 adrenergic receptor gene (Gly16Arg); and

25 (48) CAA to GAA substitution at codon 27 of the β 2 adrenergic receptor gene (Gln27Glu).

18. The kit of Claim 17, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with optic neuropathy.

5 19. A kit for diagnosing or predicting susceptibility to normal tension glaucoma in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group
10 consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

(2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

15 (5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene
20 promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(26) TTG to ATG substitution at Codon 55 of the Paraoxonase 1 gene (Leu55Met);

25 (32) GGA to CGA substitution at codon 389 of the β 1

adrenergic receptor gene (Gly389Arg);

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene (Lys119Lys).

20. The kit of Claim 19, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with normal tension glaucoma.

21. A kit for diagnosing or predicting susceptibility to primary open angle glaucoma in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

(4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of

the Optineurin gene;

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

5 (47) GGA to AGA substitution at codon 16 of the $\beta 2$ adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the $\beta 2$ adrenergic receptor gene (Gln27Glu).

10 22. The kit of claim 21, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with primary open angle glaucoma.

23. A kit for diagnosing or predicting susceptibility to Leber's disease in a human subject which comprises primer
15 set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

20 (40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro);

(41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrolase gene (Tyr113His).

24. The kit of Claim 23, wherein the set of the genetic polymorphisms further comprises at least one genetic
25 polymorphism which has been known to be associated with

Leber's disease.

25. An isolated polynucleotide consisting of a segment of the sequence:

8881 tctaagatta aaaatgccct agcccacttc ttaccacaag gcacacctac accccttatc
5 8941 cccatactag ttattatcga aaccatcagc ctactcattc aaccaatagc cctggccgta
9001 cgcctaaccg ctaacattac tgcaggccac ctactcatgc acctaattgg aagcgccacc
9061 ctagcaatat caaccattaa ccttccctct acacttatga tcttcacaat tctaattcta
9121 ctgactatcc tagaaatcgc tgtcgctta atccaagcct acgttttcac acttctagta
9181 agcctctacc tgcacgacaa cacataatga cccaccaatc acatgcctat catatagtaa

10 wherein the segment comprises at least 90 contiguous nucleotide, and the at least 90 contiguous nucleotide includes position 9099 of the sequence, and wherein position 9099 of the sequence is A, or an isolated polynucleotide which is entirely complementary to the above
15 segment.

26. An isolated polynucleotide consisting of a segment of the sequence as shown in Claim 25, wherein the segment comprises at least 90 contiguous nucleotide, and the at least 90 contiguous nucleotide includes position 9101 of
20 the sequence, and wherein position 9101 of the sequence is G, or an isolated polynucleotide which is entirely complementary to the above segment.

27. An isolated polynucleotide consisting of a segment of the sequence:

25 301 actggaaagc acgggtgctg tgggtgtactc ggggagcctc tatttccagg gcgctgagtc

361 cagaactgtc ataagatatg agctgaatac cgagacagtg aaggctgaga aggaaatccc
421 tggagctggc taccacggac agttcccgta ttcttggggg ggctacacgg acattgactt
481 ggctgtggat gaagcaggcc tctgggtcat ttacagcacc gatgaggcca aagggtgcat
541 tgtcctctcc aaactgaacc cagagaatct ggaactcgaa caaacctggg agacaaacat

5 wherein the segment comprises at least 90 contiguous
nucleotide, and the at least 90 contiguous nucleotide
includes codon 369, which is corresponding to the
underlined nucleotides of the sequence, and wherein codon
369 is substituted such that it codes for Leu, or an
10 isolated polynucleotide which is entirely complementary to
the above segment.

28. An isolated polynucleotide consisting of a segment of
the sequence:

79741 ttagttccta caatggagtc atgtctggga agaacttagg gtccaatatg agccacatgt
15 79801 caagggccag gtgtgcatca aagacaaagg gtgaagtat gagtcagagg ttggagtcac
79861 gtctgggtca aaggccagg gtcaggcttg gccatggttc catcttgatg cacaggagct
79921 gaaggacagg atgacggaac tggtgcccct gagctcggtc ctggagcagt acaaggcaga
79981 cacgcgacc attgtacgct tgccgggagga ggtgaggaat ctctccggca gtctggcggc
80041 cattcaggag gagatgggtg cctacgggta tgaggacctg cagcaacggg tgatggccct
20 80101 ggaggcccgg ctccacgcct gcgccagaa gctgggtatg ccttggccct tgaccctgac
80161 ccctgatctc tgactgccac acccaactcc agtatcacct gtttgtgcct agaagctgga
80221 cacagttttg acctctaact tttaaacttc aacccttgac cttcctacct aaggctacac

wherein the segment comprises at least 90 contiguous
nucleotide, and the at least 90 contiguous nucleotide
25 includes codon 144, which is corresponding to the

underlined nucleotides of the sequence, and wherein codon 144 is substituted such that it codes for Gln, or an isolated polynucleotide which is entirely complementary to the above segment.

5 29. A method for treating glaucoma in a patient who has an abnormality in the Myocilin gene, which comprises suppressing the expression of the abnormal Myocilin genes in the patient.

30. The method of Claim 29, wherein the suppression is
10 carried out by means of RNA interference method.

31. A method for predicting the response of a subject to the treatment with a drug, which comprises the steps of; determining genotype in respect of at least one genetic polymorphism being associated with optic neuropathy, and
15 predicting the response of the patient based on the genotype.

32. The method of Claim 31, wherein the optic neuropathy is glaucoma or Leber's disease.

33. The method of Claim 31, wherein the optic neuropathy
20 is glaucoma.

34. The method of Claim 31, wherein the at least one genetic polymorphism is 3123C>A polymorphism of the Angiotensin II type 2 receptor gene.

35. The method of Claim 31, wherein the drug is an
25 Angiotensin Receptor II antagonist.